WO 2005/014623

PCT/DK2004/000527

102

Claims

1. A compound comprising two individual peptide sequences, wherein at least one of the two sequences comprises a sequence of the formula

5

10

15

25

30

35

L1-A-L2-B-L3-C-L4-D-L5

wherein

one of A, B, C, D is selected from a hydrophobic amino acid residue, one of A, B, C, D is selected from a basic amino acid residue, Asn or Gln, one of A, B, C, D is selected from an acidic amino acid residue, Asn or Gln, one of A, B, C, D is Gly or Ala, and

L1, L2, L3, L4 and L5 is selected from a chemical bond or an amino acid sequence having n amino acid residues, wherein n is an integer of from 0 to 5, wherein

said peptide sequences are connected to each other through a linker of the formula

X[(A)nCOOH][(B)mCOOH]

20 n and m independently are an integer of from 1 to 20,

X is HN, $H_2N(CR_2)pCR$, $RHN(CR_2)pCR$, $HO(CR_2)pCR$, $HS(CR_2)pCR$, halogen-($CR_2)pCR$, $HOOC(CR_2)pCR$, $ROOC(CR_2)pCR$, $HCO(CR_2)pCR$, $RCO(CR_2)pCR$, $RCO(CR_2)$, $RCO(CR_2)$, $RCO(CR_2)$, $RCO(CR_2)$, $RCO(CR_2)$, $RCO(CR_2)$,

A and B independently are a substituted or unsubstituted C_{1-10} alkyl, a substituted or unsubstituted C_{2-10} alkenyl, a substituted or unsubstituted cyclic moiety, a substituted or unsubstituted heterocyclic moiety, a substituted or unsubstituted aromatic moiety, or A and B together form a substituted or unsubstituted cyclic moiety, substituted or unsubstituted heterocyclic moiety, or substituted or unsubstituted aromatic moiety.

2. The compound according to claim 1, wherein the at least one of the two peptide sequences is capable of binding to a functional cell surface receptor.

10

25

- The compound according to claim 2, wherein the functional cell surface receptor
 is a receptor selected from the family of fibroblast growth factor receptors
 (FGFRs) comprising FGFR1, FGFR2, FGFR3 and FGFR4, or functional homologues thereof.
- 4. The compound according to claim 2, wherein the at least one of the two peptide sequences is derived from the sequence of a polypeptide selected from the group comprising cell adhesion molecules, cell-surface receptors, heparan sulphate proteoglycans, and metalloproteases, extracellular matrix molecules or growth factors.
- 5. The compound according to the claim 4, wherein the cell adhesion molecule is selected from the group comprising
- Neural Cell Adhesion Molecule (NCAM) (Swiss-Prot Ass. Nos: P13591, P13595-01, P13595),
 - Neural cell adhesion molecule L1 (Swiss-Prot Ass. Nos: Q9QYQ7, Q9QY38, P11627, Q05695, P32004),
 - Neural Cell Adhesion Molecule-2 (NCAM-2) (Swiss-Prot Ass. No: P36335)
- Neuron-glia Cell Adhesion Molecule (Ng-CAM) (Swiss-Prot Ass. No: Q03696; Q90933),
 - Neural cell adhesion molecule CALL (Swiss-Prot Ass. No: O00533),
 - Neuroglian (Swiss-Prot Ass. No: P91767, P20241),
 - Nr-CAM (HBRAVO, NRCAM, NR-CAM 12) (Swiss-Prot Ass. Nos: Q92823, O15179, Q9QVN3
 - Axonin-1/TAG-1 (Swiss-Prot Ass. Nos: Q02246, P22063, P28685).
 - Axonal-associated Cell Adhesion Molecule (AxCAM) (NCBI Ass. No: NP_031544.1; Swiss-Prot Ass. No: Q8TC35),
 - Myelin-Associated Glycoprotein (MAG) (Swiss-Prot Ass. No: P20917),
 - Neural cell adhesion molecule BIG-1 (Swiss-Prot Ass. No: Q62682),
 - Neural cell adhesion molecule BIG-2 (Swiss-Prot Ass. No: Q62845),
 - Fasciclin (FAS-2) (Swiss-Prot Ass. No: P22648),
 - Neural cell adhesion molecule HNB-3/NB-3 (Swiss-Prot Ass. Nos: Q9UQ52, P97528, Q9JMB8)
- Neural cell adhesion molecule HNB-2/NB-2 (Swiss-Prot Ass. Nos: O94779,

P07409, P97527),

25

- Cadherin (Swiss-Prot Ass. No: Q9VW71),
- Junctional Adhesion Molecule-1 (JAM-1) (Swiss-Prot Ass. Nos: Q9JKD5, O88792),
- Neural cell adhesion F3/F11(Contactin) (Swiss-Prot Ass. Nos: Q63198, P1260,
 Q12860, Q28106, P14781, O93250),
 - Neurofascin (Swiss-Prot Ass. Nos: Q90924, Q91Z60; O42414),
 - B-lymphocyte cell adhesion molecule CD22 (Swiss-Prot Ass. Nos: Q9R094, P20273),
- Neogenin (NEO1) (Swiss-Prot Ass. Nos: Q92859, P97603, Q90610, P97798).
 - Intercellular Cell Adhesion Molecule-5 (ICAM-5/telencephalin) (Swiss-Prot Ass. Nos: Q8TAM9, Q60625) or
 - Galactose binding lectin-12 (galectin-12) (Swiss-Prot Ass. Nos: Q91VD1, Q9JKX2, Q9NZ03),
- Galactose binding lectin-4 (galectin-4) (Swiss-Prot Ass. No: Q8K419; P38552),
 or fragments, or variants thereof.
 - 6. The compound according to the claim 4, wherein the cell-surface receptor is selected from the group comprising
- Fibroblast Growth Factor Receptor 1 (FGFR1) (Swiss-Prot Ass. Nos: Q9QZM7,
 Q99AVV7, Q9UD50, Q63827),
 - Fibroblast Growth Factor Receptor 2 (FGFR2) (Swiss-Prot Ass. Nos: Q96KM2, P21802, Q63241),
 - Fibroblast Growth Factor Receptor 3 (FGFR3) (Swiss-Prot Ass. Nos: Q95M13, AF487554, Q99052),
 - Fibroblast Growth Factor Receptor 4 (FGFR4) (Swiss-Prot Ass. No: Q91742),
 - Neurotrophin Tyrosin Kinase Type-2 (NTRKT-2) (Swiss-Prot Ass. No: Q8WXJ5),
 - Leukocyte Antigen Related Protein-Tyrosine Phosphatase (LAR-PTPRF) (Swiss-Prot Ass. Nos: Q9EQ17, Q64605, Q64604, Q9QW67, Q9VIS8 P10586),
 - Nephrin (Swiss-Prot Ass. Nos: Q925S5, Q9JIX2, Q9ET59, Q9R044, Q9QZS7, Q06500),
- Protein-Tyrosine Phosphatase Receptor type S (PTPRS) (Swiss-Prot Ass. Nos: Q64699, Q13332, O75870),

WO 2005/014623

15

35

105

PCT/DK2004/000527

- Protein-Tyrosine Phosphatase Receptor type kappa (R-PTP-kappa) (Swiss-Prot Ass. No: Q15262),
- Protein-Tyrosine Phosphatase Receptor type D (PTPRD) (Swiss-Prot Ass. Nos: Q8WX65, Q9IAJ1, P23468, Q64487).
- Ephrin type-A receptor 8 (EPHA8/Tyrosine-Protein Kinase Receptor EEK)
 (Swiss-Prot Ass. Nos: O09127, P29322),
 - Ephrin type-A receptor 3 (EPHA8/Tyrosine-Protein Kinase Receptor ETK-1/CEK4) (Swiss-Prot Ass. No: P29318),
 - Ephrin type-A receptor 2 (Swiss-Prot Ass. No: Q8N3Z2)
- Insulin Receptor (IR) (Swiss-Prot Ass. No: Q9PWN6)
 - Insulin-like Growth Factor-1 Receptor (IGF-1) (Swiss-Prot Ass. Nos: Q9QVW4, P08069, P24062, Q60751, P15127, P15208)
 - Insulin-related Receptor (IRR) (Swiss-Prot Ass. No: P14616),
 - -Tyrosine-Protein Kinase Receptor Tie-1 (Swiss-Prot Ass. Nos: 06805, P35590, Q06806).
 - Roundabout receptor-1 (robo-1) (Swiss-Prot Ass. Nos: O44924, AF041082, Q9Y6N7),
 - Neuronal nicotinic acetylcholine receptor alpha 3 subunit (CHRNA3) (Swiss-Prot Ass. Nos: Q8VHH6, P04757, Q8R4G9, P32297)
- Neuronal acetylcholine receptor alpha 6 subunit (Swiss-Prot Ass. Nos: Q15825, Q9R0W9)
 - Platelet-Derived Growth Factor Receptor Beta (PDGFRB) (Swiss-Prot Ass. Nos: Q8R406, Q05030),
 - Interleukin-6 Receptor (IL-6R) (Swiss-Prot Ass. No: Q00560),
- Interleukin-23 Receptor (IL-23R) (Swiss-Prot Ass. No: AF461422),
 - Beta-common cytokine receptor of IL-3, IL5 and GmCsf (Swiss-Prot Ass. No: P32927)
 - Cytokine Receptor-Like molecule 3 (CRLF1) (Swiss-Prot Ass. No: Q9JM58),
 - Class I Cytokine Receptor (ZCYTOR5) (Swiss-Prot Ass. No: Q9UHH5)
- Netrin-1 receptor DCC (Swiss-Prot Ass. No: P43146),
 - Leukocyte Fc Receptor-like Protein (IFGP2) (Swiss-Prot Ass. Nos: Q96PJ6, Q96KM2),
 - Macrophage Scavenger Receptor 2 (MSR2) (Swiss-Prot Ass. No: Q91YK7), or
 - Granulocyte Colony Stimulating Factor Receptor (G-CSF-R) (Swiss-Prot Ass. No: Q99062),

106

or fragments, or variants thereof.

- 7. The compound according to the claim 4, wherein the heparan sulphate proteoglycan is perlecan (Swiss-Prot Ass. No: P98160), or a fragment, or a variant thereof.
- 8. The compound according to the claim 4, wherein the metalloprotease is selected from the group comprising
 - ADAM-8 (Swiss-Prot Ass. No: Q05910),
- 10 ADAM-19 (Swiss-Prot Ass. Nos: Q9H013, O35674),
 - ADAM-8 (Swiss-Prot Ass. No: P78325),
 - ADAM-12 (Swiss-Prot Ass. Nos: O43184, Q61824),
 - ADAM-28 (Swiss-Prot Ass. Nos: Q9JLN6, Q61824, Q9XSL6, Q9UKQ2),
 - ADAM-33 precursor (Swiss-Prot Ass. Nos: Q8R533, Q923W9),
- 15 ADAM-9 (Swiss-Prot Ass. Nos: Q13433, Q61072),
 - ADAM-7 (Swiss-Prot Ass. NoS: Q9H2U9, O35227, Q63180),
 - ADAM-1A Fertilin alpha (Swiss-Prot Ass. No: Q8R533),
 - ADAM-15 (Swiss-Prot Ass. Nos: Q9QYV0, O88839, Q13444),
 - Metalloproteinase-desintegrin domain containing protein (TECAM) (Swiss-Prot Ass. No: AF163291),
 - Metalloproteinase 1 (Swiss-Prot Ass. Nos: O95204, Q9BSI6), or fragments, or variants thereof.
 - 9. The compound according to the claim 4, wherein the extracellular matrix molecule is selected from the group comprising
 - Collagen type VII (Swiss-Prot Ass. No: Q63870),
 - Fibronectin (Swiss-Prot Ass. Nos: Q95KV4, Q95KV5, P07589, Q28377, U42594, O95609, P11276), or
 - Tenascin-R (Swiss-Prot Ass. Nos: Q15568, O00531, Q90995, P10039), or fragments, or variants thereof.
 - 10. The compound according to the claim 4, wherein the growth factor is Cytokine-like factor-1 (CLF-1) (Swiss-Prot Ass. No:O75462), or a fragment, or a variant thereof.

30

20

25

	107
	11. The compound according to any of the claims 1 to 10, wherein the at least one
	of the two peptide sequences is a peptide fragment having the amino acid se-
	quence selected from
	EVYVVAENQQGKSKA (SEQ ID NO 1),
5	NIEVWVEAENALGKKV (SEQ ID NO: 2),
	ATNRQGKVKAFAHL (SEQ ID NO: 3),
	RYVELYVVADSQEFQK (SEQ ID NO: 4)
	VAENSRGKNVAKG (SEQ ID NO: 5),
	GEYWCVAENQYGQR (SEQ ID NO: 6),
10	RLAALNGKGLGEIS (SEQ ID NO: 7),
	KYIAENMKAQNVAKEI (SEQ ID NO: 8),
	TIMGLKPETRYAVR (SEQ ID NO: 9),
	KGLGEISAATEFKT (SEQ ID NO: 10),
	NMGIWVQAENALG (SEQ ID NO: 11),
15	IWVQAENMLG (SEQ ID NO: 12),
	EIWVEATNRLG (SEQ ID NO: 13),
	VWVQAANALG (SEQ ID NO: 14),
	EVWIEKDPAKGRI (SEQ ID NO: 15),
	ATNKGGEVKKNGHL (SEQ ID NO: 16),
20	KYVELYLVADYLEFQK (SEQ ID NO: 17),
	RYVELYVVVDNAEFQ (SEQ ID NO: 18),
	KYVELVIVADNREFQR (SEQ ID NO: 19),
	KYIEYYLVLDNGEFKR (SEQ ID NO: 20),
	RYLELYIVADHTLF (SEQ ID NO: 21),
25	KYVEMFVVVNHQRFQ (SEQ ID NO: 22),
	RYVELFIVVDKERY (SEQ ID NO: 23),
	KYVELFIVADDTVYRR (SEQ ID NO: 24),
	KFIELFVVADEYVYRR (SEQ ID NO: 25),
	KIVEKVIVADNSEVRK (SEQ ID NO: 26),
30	VELVIVADHSEAQK (SEQ ID NO: 27),
	VAENSRGKNIAKG (SEQ ID NO: 28),
	IAENSRGKNVARG (SEQ ID NO: 29),
	AENSRGKNSFRG (SEQ ID NO: 30),
	IASNLRGRNLAKG (SEQ ID NO: 31),
35	IPENSLGKTYAKG (SEQ ID NO: 32),

	IAENMKAQNEAK (SEQ ID NO: 33),
	QFIAENMKSHNETKEV (SEQ ID NO: 34)
	GEYWCVAKNRVGQ (SEQ ID NO: 35),
	GSYTCVAENMVGK (SEQ ID NO: 36),
5	GKYVCVGTNMVGER (SEQ ID NO: 37),
	GNYTCVVENEYG (SEQ ID NO: 38),
	GEYTCLAGNSIG (SEQ ID NO: 39),
	QYYCVAENGYG (SEQ ID NO: 40),
	GEYYQEAEQNGYG (SEQ ID NO: 41),
10	GNYTCLVENEYG (SEQ ID NO: 42),
	GMYQCLAENAYG (SEQ ID NO: 43),
	GMYQCAENTHG (SEQ ID NO: 44),
	GIYYCLASNNYG (SEQ ID NO: 45),
	GGYYCTADNSYG (SEQ ID NO: 46),
15	GEYQCFARNDYG (SEQ ID NO: 47),
	GEYFCLASNKMG (SEQ ID NO: 48),
	GEYQCFARNKFG (SEQ ID NO: 49),
	GEYFCLASNKMG (SEQ ID NO: 50),
	GGYYCTADNNYG (SEQ ID NO: 51),
20	GNYSCEAENAWGTK (SEQ ID NO: 52),
	GEYTCLAENSLG (SEQ ID NO: 53),
	GEYECVAENGRLG (SEQ ID NO: 54),
	GNYTCVVENKFGR (SEQ ID NO: 55),
	GEYTCLAGNSIG (SEQ ID NO: 56),
25	GEYFCVASNPIG (SEQ ID NO: 57),
	EYTCIANNQAGE (SEQ ID NO: 58),
	GMYQCVAENKHLG (SEQ ID NO: 59),
	GEYMCTASNTIGQ (SEQ ID NO: 60),
	EYVCIAENKAGEQ (SEQ ID NO: 61),
30	GDYTLIAKNEYGK (SEQ ID NO: 62),
	GFYQCVAENEAG (SEQ ID NO: 63),
	GKYECVATNSAGTR (SEQ ID NO: 64),
	GEYFCVYNNSLG (SEQ ID NO: 65),
	GEYECAATNAHGR (SEQ ID NO: 66),
35	GAYWCQGTNSVGK (SEQ ID NO: 67),

109

GTYSCVAENILG (SEQ ID NO: 68), RVAAVNGKGQGDYS (SEQ ID NO: 69),

RVAAINGCGIGPFS (SEQ ID NO: 70),

AVLNGKGLG (SEQ ID NO: 71),

5 ALNGQGLGATS (SEQ ID NO: 72),

RLAAKNRAGLGE (SEQ ID NO: 73),

RLGVVTGKDLGEI (SEQ ID NO: 74),

TVTGLKPETSYMVK (SEQ ID NO: 75),

TLTGLKPSTRYRI (SEQ ID NO: 76),

10 TLTGLQPSTRYRV (SEQ ID NO: 77),

TLLGLKPDTTYDIK (SEQ ID NO: 78),

TLQGLRPETAYELR (SEQ ID NO: 79),

TLRGLRPETAYELR (SEQ ID NO: 80),

TLMNLRPKTGYSVR (SEQ ID NO: 81),

15 TVSGLKPGTRY (SEQ ID NO: 82),

TISGLKPDTTY (SEQ ID NO: 83),

TLQGLKPDTAY (SEQ ID NO: 84),

LRGLKPWTQYAV (SEQ ID NO: 85),

IDGLEPDTEYIVR (SEQ ID NO: 86),

20 LQGLKPWTQYAI (SEQ ID NO: 87),

TITGLEPGTEYTIQ (SEQ ID NO: 88),

GLKPWTQYAV (SEQ ID NO: 89),

TLASLKPWTQYAV (SEQ ID NO: 90),

LMGLQPATEYIV (SEQ ID NO: 91),

25 KGMGPMSEAVQFRT (SEQ ID NO: 92),

TLTGLKPDTTYDVK (SEQ ID NO: 93),

ISGLQPETSYSL (SEQ ID NO: 94),

TLLGLKPDTTYDIK (SEQ ID NO: 95),

TISGLTPETTYSI (SEQ ID NO: 96),

30 GNYSCLAENRLGR (SEQ ID NO: 97),

GNYTCVVENRVG (SEQ ID NO: 98),

GTYHCVATNAHG (SEQ ID NO: 99),

LSHNGVLTGYLLSY (SEQ ID NO: 100),

NGVLTGYVLRY (SEQ ID NO: 101),

35 NGVLTGYNLRY (SEQ ID NO: 102),

110

NGNLTGYLLQY (SEQ ID NO: 103), VDENGVLTGYKIYY (SEQ ID NO: 104),

THNGALVGYSVRY (SEQ ID NO: 105),

NGILTEYILKY (SEQ ID NO: 106),

5 NGILIGYTLRY (SEQ ID NO: 107),

THSGQITGYKIRY (SEQ ID NO: 108),

NGKITGYIIYY (SEQ ID NO: 109),

LSHNGIFTLY (SEQ ID NO: 110),

NGILTEYTLKY (SEQ ID NO: 111),

10 LDPNGIITQYEISY (SEQ ID NO: 112),

NGKITGYIIYY (SEQ ID NO: 113),

HLEVQAFNGRGSGPA (SEQ ID NO: 114),

HLTVRAYNGAGYGP (SEQ ID NO: 115),

HLSVKAYNSAGTGPS (SEQ ID NO: 116),

15 HLAVKAYNSAGTGPS (SEQ ID NO: 117),

NLEVRAFNSAGDGP (SEQ ID NO: 118),

HLTVLAYNSKGAGP (SEQ ID NO: 119),

LRVLVFNGRGDGP (SEQ ID NO: 120),

HIDVSAFNSAGYGP (SEQ ID NO: 121),

20 HLAVELFNGR (SEQ ID NO: 122),

LELQSINFLGGQPA (SEQ ID NO: 123),

HFTVRAYNGAGYGP (SEQ ID NO: 124),

HLEVQAFNGRGSQPA (SEQ ID NO: 125),

VIADQPTFVKYLIK (SEQ ID NO: 126),

25 TIKGLRPGVVYEGQ (SEQ ID NO: 127),

TLTELSPSTQYTVK (SEQ ID NO: 128),

TLDDLAPDTTYLVQ (SEQ ID NO: 129),

TVSDVTPHAIYTVR (SEQ ID NO: 130),

IIRGLNASTRYLFR (SEQ ID NO:131),

30 TLMNLRPKTGYSVR (SEQ ID NO:132),

TLTGLKPGTEYEVR (SEQ ID NO: 133),

GPEHLMPSSTYVAR (SEQ ID NO: 134),

RVTGLTPKKTYEFR (SEQ ID NO: 135),

LTGLKPGTEYEFR (SEQ ID NO: 136),

35 EVRVQAVNGGGNGPP (SEQ ID NO: 137),

1 .

111

LIKVVAINDRGE (SEQ ID NO: 138),

VVSIIAVNGREE (SEQ ID NO: 139),

VVSVYAQNQNGE (SEQ ID NO: 140),

TISLVAEKGRHK (SEQ ID NO: 141),

5 HLEVQAFNGRGSGPA (SEQ ID NO: 142),

HVEVQAFNGRGLGPA (SEQ ID NO: 143).

HVEVQAFNGRGLGPA (SEQ ID NO: 144),

EFRVRAVNGAGEG (SEQ ID NO: 145), or

VARVRTRLAPGSRLS (SEQ ID NO: 146), or

or a fragment, or a variant, or homologue thereof.

- 12. The compound according to claims 1 to 10, wherein the at least one of the two peptide sequences is SEQ ID NO: 1 (EVYVVAENQQGKSKA), or a fragment, variant, or homologue of said sequence.
- 13. The compound of claim 12, wherein the variant or homologue of SEQ ID NO: 1 is selected from SEQ ID NOs: 2-9, 100 or 125,
- 14. The compound according to claims 1 to 10, wherein the at least one of the two peptide sequences is SEQ ID NO: 2 (NIEVWVEAENALGKKV), or a fragment, variant or homologue of said sequence.
 - 15. The compound according to any of the preceding claims, wherein the compound comprises two individual peptide fragments comprising different amino acid sequences, said different amino acid sequences being selected from any of the peptide fragments of claim 11.
 - 16. The compound according to any of the preceding claims, wherein the compound comprises two peptide fragments comprising the identical amino acid sequence, said amino acid sequence being selected from any of the peptide fragments of claim 11.
 - 17. The compound according to claim 16, wherein the peptide fragments are independently having the sequence EVYVVAENQQGKSKA (SEQ ID NO: 1).

30

25

10

15

20

25

30

- 18. The compound according to claim 16, wherein the peptide fragments are independently having the sequence NIEVWVEAENALGKKV (SEQ ID NO: 2).
- 19. The compound according to claim 15, wherein one of the two peptide fragments is having the sequence EVYVVAENQQGKSKA (SEQ ID NO: 1), and the other is having the sequence NIEVWVEAENALGKKV (SEQ ID NO: 2).
- 20. The compound according to any of the preceding claims, said compound being obtained by a method for preparing an LPA enabling presentation of sequence(s) as defined in claim 11 comprising the steps of
 - (a) providing by solid phase synthesis or fragment coupling ligands comprising desired sequence(s), the ligands being attached to a solid phase.
 - (b) if nessesary, deprotecting any N-terminal amino acid groups while th eligands/s) are still attached to the solid phase,
 - (c) reacting the ligand(s) having unprotected N-terminal groups with an achiral di- tri- or tetracarboxylic acid so as to provide a construct having a ring structure, and
 - (d) cleaving the construct from the solid phase so as to provide an LPA comprising ligands having free C-terminal groups.
- 21. A pharmaceutical composition comprising a compound as defined in claims 1-20.
- 22. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for treatment of conditions of the central and peripheral nervous system associated with postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, postischaemic damage, e.g. resulting from a stroke, Parkinson's disease, Alzheimer's disease, Huntington's disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia, mood disorders, such as manic depression; for treatment of diseases or conditions of the muscles including conditions with impaired function of neuro-muscular connections, such as after organ transplantation, or such as genetic or traumatic atrophic muscle disorders; or for treatment of diseases or conditions of various organs, such as degenerative conditions of

10

20

30

the gonads, of the pancreas such as diabetes mellitus type I and II, of the kidney such as nephrosis and of the heart, liver and bowel.

- 23. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the treatment of postoperative nerve damage, traumatic nerve damage, impaired myelination of nerve fibers, postischaemic, e.g. resulting from a stroke, Parkinson's disease, Alzheimer's disease, Huntington's disease, dementias such as multiinfarct dementia, sclerosis, nerve degeneration associated with diabetes mellitus, disorders affecting the circadian clock or neuro-muscular transmission, and schizophrenia, mood disorders, such as manic depression.
- 24. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the promotion of wound-healing.
- 15 25. Use a compound as defined in claims 1-20 for the manufacture of a medicament for the treatment of cancer
 - 26. The use according to claim 25, wherein the cancer is any type of solid tumors requiring neoanglogenesis
 - 27. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the prevention of death of heart muscle cells, such as after acute myocardial infarction, or after angiogenesis
- 25 28. Use a compound as defined in any of claims 1-20 for the manufacture of a medicament for revascular sation.
 - 29. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the stimulation of the ability to learn and/or the short and/or long-term memory
 - 30. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the prevention of cell death due to ischemia.

114

- 31. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the prevention of body damages due to alcohol consumption.
- 32. Use a compound as defined in any of the claims 1-20 for the manufacture of a medicament for the treatment of prion diseases.
 - 33. Use of a medicament of any of the claims 22-31 or pharmaceutical composition according to claim 21 for the treatment of a disease or condition as defined in claims 22-31.

10

5

34. A method of treatment of an individual in need comprising a step of administering to said individual a compound as defined in any of the claims 1 to 20, and/or a pharmaceutical composition as defined in claim 21, and/or medicament as defined in claims 22-31.